Bullous Dermatoses and Quality of Life: A Summary of Tools to Assess Psychosocial Health

Alexandria Riopelle, MD; Eden Lake, MD

PRACTICE POINTS

- Autoimmune bullous dermatoses cause cutaneous lesions that are painful and disfiguring. These conditions affect a patient's ability to perform everyday tasks, and individual lesions can take years to heal.
- Providers should take necessary steps to address patient well-being, especially at disease onset in patients with bullous dermatoses.

Autoimmune bullous dermatoses (ABDs), such as pemphigus and bullous pemphigoid (BP), cause cutaneous lesions that are painful and disfiguring. These conditions affect a patient's ability to perform everyday tasks, and individual lesions can take years to heal. Multiple small studies have examined how these conditions affect a patient's lifestyle. We systematically reviewed the trials that have evaluated the mental health of patients with bullous dermatoses. Of the 13 studies assessed, 2 domains of interest were primarily evaluated: quality of life (QOL) and psychological state. Quality of life predominantly was analyzed using the Dermatology Life Quality Index (DLQI). To evaluate psychological state, the General Health Questionnaire (GHQ) primarily was utilized. This review informs providers and summarizes the various ways that ABDs affect mental health.

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due to antibodies directed against antigens within the epidermis or at the dermoepidermal junction. They are categorized histologically by the location of acantholysis (separation of keratinocytes), clinical presentation, and presence of autoantibodies. The most common

ABDs include pemphigus vulgaris, pemphigus foliaceus, and bullous pemphigoid (BP). These conditions present on a spectrum of symptoms and severity.¹

Although multiple studies have evaluated the impact of bullous dermatoses on mental health, most were designed with a small sample size, thus limiting the generalizability of each study. Sebaratnam et al² summarized several studies in 2012. In this review, we will analyze additional relevant literature and systematically combine the data to determine the psychological burden of disease of ABDs. We also will discuss the existing questionnaires frequently used in the dermatology setting to assess adverse psychosocial symptoms.

Methods

We searched PubMed, MEDLINE, and Google Scholar for articles published within the last 15 years using the terms *bullous pemphigoid, pemphigus, quality of life, anxiety,* and *depression*. We reviewed the citations in each article to further our search.

Criteria for Inclusion and Exclusion—Studies that utilized validated questionnaires to evaluate the effects of pemphigus vulgaris, pemphigus foliaceus, and/or BP on mental health were included. All research participants were 18 years and older. For the questionnaires administered, each study must have included numerical scores in the results. The studies all reported statistically significant results (P<.05), but no studies were excluded on the basis of statistical significance.

Studies were excluded if they did not use a validated questionnaire to examine quality of life (QOL) or psychological status. We also excluded database, retrospective, qualitative, and observational studies. We did not include

Dr. Riopelle is from the Department of Dermatology, Boston Medical Center, Massachusetts. Dr. Lake is from the Division of Dermatology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois.

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Correspondence: Alexandria Riopelle, MD, 609 Albany St, Boston, MA 02118 (LexiRiopelle@gmail.com). doi:10.12788/cutis.0439

studies with a sample size less than 20. Studies that administered questionnaires that were uncommon in this realm of research such as the Attitude to Appearance Scale or The Anxiety Questionnaire also were excluded. We did not exclude articles based on their primary language.

Results

A total of 13 studies met the inclusion criteria with a total of 1716 participants enrolled in the trials. The questionnaires most commonly used are summarized in Table 1. Tables 2 and 3 demonstrate the studies that evaluate QOL and psychological state in patients with bullous dermatoses, respectively.

The Dermatology Life Quality Index (DLQI) was the most utilized method for analyzing QOL followed by the Skindex-17, Skindex-29, and 36-Item Short Form Health Survey. The DLQI is a skin-specific measurement tool with higher scores translating to greater impairment in QOL. Healthy patients have an average score of 0.5.3 The mean DLQI scores for ABD patients as seen in Table 2 were 9.45, 10.18, 16, 10.9, and 10.1. 13-15,18,22 The most commonly reported concerns among patients included feelings about appearance and disturbances in daily activities.¹⁸ Symptoms of mucosal involvement, itching, and burning also were indicators of lower QOL. 15,18,20,22 Furthermore, women consistently had lower scores than men. 15,17,19,25 Multiple studies concluded that severity of the disease correlated with a lower QOL, though the subtype of pemphigus did not have an effect on QOL scores. 15,19,20,21 Lastly, recent onset of symptoms was associated with a worse QOL score. 15,18-20 Age, education level, and marital status did not have an effect on QOL.

To evaluate psychological state, the General Health Questionnaire (GHQ)-28 and -12 primarily were used, in addition to the Hospital Anxiety and Depression Scale; the *International Classification of Diseases, Tenth Revision;* the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition;* and the Beck Depression Inventory-II. As seen in Table 3, GHQ-12 positivity, reflecting probable minor nonpsychotic psychiatric disorders such as depression and anxiety, was identified in 47%, 39.7%, and 40% of patients with pemphigus patients. In the average population, GHQ positivity was found in up to 12% of patients. Similar to the QOL scores, no significant differences were seen based on subtype of pemphigus for symptoms of depression or anxiety. Similar to the content of the positivity of pemphigus for symptoms of depression or anxiety.

Comment

Mental Health of Patients With ABDs—Immunobullous diseases are painful, potentially lifelong conditions that have no definitive cure. These conditions are characterized by bullae and erosions of the skin and mucosae that physically are disabling and often create a stigma for patients. Across multiple different validated psychosocial assessments, the 13 studies included in this review consistently reported that ABDs have a negative effect on

mental well-being of patients that is more pronounced in women and worse at the onset of symptoms. ¹³⁻²⁵

QOL Scores in Patients With ABDs-Quality of life is a broad term that encompasses a general sense of psychological and overall well-being. A score of approximately 10 on the DLQI most often was reported in patients with ABDs, which translates to a moderate impact on QOL. In comparison, a large cohort study reported the mean (SD) DLQI scores for patients with atopic dermatitis and psoriasis as 7.31 (5.98) and 5.93 (5.66), respectively.²⁸ In another study, Penha et al14 found that patients with psoriasis have a mean DLQI score of 10. Reasons for the similarly low QOL scores in patients with ABDs include long hospitalization periods, disease chronicity, social anxiety, inability to control symptoms, difficulty with activities of daily living, and the belief that the disease is incurable. 17,19,23 Although there is a need for increased family and social support with performing necessary daily tasks, personal relationships often are negatively affected, resulting in social isolation, loneliness, and worsening of cutaneous symptoms.

Severity of cutaneous disease and recent onset of symptoms correlated with worse QOL scores. Tabolli et al²⁰ proposed the reason for this relates to not having had enough time to find the best treatment regimen. We believe there also may be an element of habituation involved, whereby patients become accustomed to the appearance of the lesions over time and therefore they become less distressing. Interestingly, Tabolli et al¹⁷ determined that patients in the quiescent phase of the disease-without any mucosal or cutaneous lesionsstill maintained lower QOL scores than the average population, particularly on the psychosocial section of the 36-Item Short Form Health Survey, which may be due to a concern of disease relapse or from adverse effects of treatment. Providers should monitor patients for mental health complications not only in the disease infancy but throughout the disease course.

Future Directions—Cause and effect of the relationship between the psychosocial variables and ABD disease state has yet to be determined. Most studies included in this review were cross-sectional in design. Although many studies concluded that bullous dermatoses were the cause of impaired QOL, Ren and colleagues²⁹ proposed that medications used to treat neuropsychiatric disorders may trigger the autoimmune antigens of BP. Possible triggers for BP have been reported including hydrochlorothiazide, ciprofloxacin, and dipeptidyl peptidase-4 inhibitors.^{27,30-32} A longitudinal study design would better evaluate the causal relationship.

The effects of the medications were included in 2 cases, one in which the steroid dose was not found to have a significant impact on rates of depression²³ and another in which patients treated with a higher dose of corticosteroids (>10 mg) had worse QOL scores.¹⁷ Sung et al¹⁵ suggested this may be because patients who took higher doses of steroids had worse symptoms

TABLE 1. Mental Health Questionnaires in a Dermatology Setting

Survey	urvey Domains of interest Scoring		Average person score	
Dermatology Life	Number of questions: 10	Each question has a score of 0–3; final	0.5	
Quality Index ³	Symptoms and feelings	score of 0-30; higher score indicates greater impairment on QOL		
	Daily activities	groater impairment on QOL		
	• Leisure			
	Personal relationships			
	 Work and school 			
	Treatment			
General Health	Number of questions: 28ª	Each question has a 4-point scale;	0%-12% GHQ+	
Questionnaire-28 ^{4,5}	Depression	final score of 0–28; GHQ+ (score >6) is probable minor psychiatric disorder		
	Anxiety	(4 if using binary scoring)		
	Social impairment			
	Hypochondriasis			
Hospital Anxiety and Depression Scale ⁶	Number of questions: 14	Response to items on a 4-point	Total=9.1; anxiety=5.1; depression=3.9	
	Designed to detect anxiety	Likert scale, ranging from 0 to 3; final score of 0-21; score >11 indicates		
	and depression	likely anxiety or depression	2.00.000.011	
UCLA Loneliness Scale ⁷	Number of questions: 20	Response based on 4-point scale; final	Young=40.08; old=31.51	
	Evaluates loneliness and	score of 20–80; higher score signifies increased perceived loneliness		
	social isolation	indicasca perceived forteliness		
Beck Depression	Number of questions: 21	Each question scored from	12.56	
Inventory-II (BDI-II)8,9	Questions regarding symptoms of	0–3; for depression, a score of 0–15=none or minimal, 16–30=mild,		
	depression, such as hopelessness	31–46=moderate, 47–63=severe		
	and irritability	·		
Skindex-29 ^{10,11}	Number of questions: 29 ^b	Responses range from never (score	35.2	
	• Assesses symptom burden,	of 0) to all the time (score of 4); total scores range from 0-100; higher		
	functioning, and emotional state	score indicates worse QOL in a dermatology setting		
36-Item Short Form Health Survey ¹²	Number of questions: 36	Scores range from 0–100; higher	No global or overall score available	
	Functioning (eg, bathing)	score indicates better health status		
	Role-playing	and better QOL; there are 8 separate scale scores		
	Bodily pain			
	General health			
	• Vitality			
	Social functioning			
	Role-emotional			
	Mental health			

Abbreviations: GHQ+, General Health Questionnaire positivity; QOL, quality of life.

^aThe GHQ-12 is a similar questionnaire with only 12 questions.

^bThe Skindex-17 is a reduced version of the Skindex-29. It has 17 questions given on a 3-point scale with higher scores indicating a worse QOL. The average person score is based off a population with dermatology conditions such as psoriasis.¹¹

TABLE 2. Trials Evaluating Bullous Dermatoses and Quality of Life

Reference (year)	Population and diagnosis, n	Mean age (SD), y	Recruitment source	Evaluation	Results and study conclusions of the bullous dermatoses cohort
Kouris et al ¹³ (2016)	57 BP, 57 healthy	59.73 (10.77)	Greek tertiary center	DLQI, UCLA Loneliness Scale	Mean (SD) BP DLQI score=9.45 (3.34); mean (SD) UCLA Loneliness Scale=43.01 (5.66)
Penha et al ¹⁴ (2015)	43 PF, 32 PV, 6 BP, 3 dermatitis herpetiformis	48 (16)	Public university service, outpatient	DLQI	Mean DLQI score=16 (classified as severe impairment of QOL)
Sung et al ¹⁵ (2015)	40 PV, 26 PF	51.1 (13.5)	Korean outpatient	DLQI	Mean DLQI for all patients=10.18; mean DLQI active disease=13.45; mean DLQI in remission=5.15
Moon et al ¹⁶ (2014)	40 PV, PF, BP, bullosa acquisita	Not reported	Not reported	Skindex-29	Mean Skindex-29 scores higher in patients with bullous dermatoses than in healthy controls
Tabolli et al ¹⁷ (2014)	47 PV/PF without bullae or erosions	52.7	Italian research hospital	Skindex-17	QOL scores were 30% lower in patients with active disease
Ghodsi et al ¹⁸ (2012)	61 newly diagnosed nontreated PV	44.1 (15)	Inpatient, Iran	DLQI	Mean (SD) DLQI score=10.9 (6.9); QOL worse in those with nasal and pharynx involvement, positive Nikolsky, severe skin involvement, and itching
Paradisi et al ¹⁹ (2009)	112 PV, 10 PF, and 4 with paraneoplastic and IgA pemphigus	PV=52.2; PF=55.1	Inpatient hospital, Italy	Skindex-29, SF-36	Skindex-29 mean score=37 (control=8), emotions=37 (control=14), functioning=33 (control=4); SF-36 showed females, older age, and mucocutaneous involvement were more likely to have worse QOL
Tabolli et al ²⁰ (2008)	58 PV/PF	Not reported	Inpatient, outpatient, Italy	SF-36	Increased mucocutaneous lesions had lower SF-36 scores
Terrab et al ²¹ (2005)	30 PV/PF, 60 controls	Not reported	Morocco dermatology clinic/inpatient	SF-36	Greatest impairment was seen in the physical and emotional states; 45% of patients reported psychological distress
Mayrshofer et al ²² (2005)	27 PV	Not reported	Not reported	DLQI	Mean (SD) DLQI score=10.1 (6.6); mucosal involvement, itching, and burning were indicators of lower QOL

Abbreviations: BP, bullous pemphigoid; DLQI, Dermatology Life Quality Index; PF, pemphigus foliaceus; PV, pemphigus vulgaris; QOL, quality of life; SF-36, 36-Item Short Form Health Survey.

and therefore also had a worse QOL. It also is possible that those patients taking higher doses had increased side effects.¹⁷ Further studies that evaluate treatment modalities and timing in relation to the disease onset would be helpful.

Study Limitations—There are potential barriers to combining these data. Multiple different questionnaires were used, and it was difficult to ascertain if all the participants

were experiencing active disease. Additionally, questionnaires are not always the best proxy for what is happening in everyday life. Lastly, the sample size of each individual study was small, and the studies only included adults.

Conclusion

As demonstrated by the 13 studies in this review, patients with ABDs have lower QOL scores and higher numbers

TABLE 3. Trials Evaluating Bullous Dermatoses and Psychological State

Reference (year)	Population, n	Mean age (SD), y	Recruitment source	Evaluation	Scores and study conclusions of the bullous dermatoses cohort
Kouris et al ¹³ (2015)	57 BP, 57 healthy	59.73 (10.77)	Greek tertiary referral center	HADS	HADS total (mean [SD], 16.1 [7.4]), and HADS depression subscale (mean [SD], 7.3 [3.8])
Sung et al ¹⁵ (2015)	40 PV, 26 PF	51.1 (13.5)	Korean outpatient	GHQ-12	GHQ+ for patients with PV and PF=47%
Layegh et al ²³ (2014)	55 PV/PF	42.34 (18.98)	Inpatients, Iran	BDI-II	28% of patients with PV and depression; 20% of patients with PF and depression
Tabolli et al ¹⁷ (2014)	47 PV/PF without bullae or erosions	52.7	Italian research hospital	GHQ-12	GHQ+ 44% lower in patients without cutaneous or mucosal lesions (not statistically significant)
Kumar et al ²⁴ (2013)	50 PV/PF, 30 psoriasis, 30 healthy	35–54	Inpatient population at a teaching hospital in North India	GHQ-12, ICD-10 diagnosis	GHQ-12+ 40%; psychiatric ICD-10 diagnoses in 26% of patients, including adjustment disorder (16%), depressive episode (8%), and acute and transient psychosis (2%); patients with pemphigus scored higher on disability and emotional outlet, and lower for anger and QOL than psoriasis
Ghodsi et al ¹⁸ (2012)	61 newly diagnosed non-treated PV	44.1 (15)	Inpatient, Iran	GHQ-28	77% experienced anxiety and depression; initial stages of disease may have greatest impact; GHQ-28+ in 77.5%
Mazzotti et al ²⁵ (2011)	74 PF/PV	48.8 (14.2)	Inpatient hospital in Rome, Italy	HADS	52.7% of patients with pemphigus reported psychological distress and rates were higher in women
Paradisi et al ¹⁹ (2009)	112 PV, 10 PF, and 4 paraneoplastic and IgA pemphigus	PV=52.2, PF= 55.1	Inpatient hospital in Rome, Italy	GHQ-12	GHQ-12+ 39.7%

Abbreviations: BDI-II, Beck Depression Inventory-II; BP, bullous pemphigoid; GHQ, General Health Questionnaire; GHQ+, General Health Questionnaire positivity; HADS, Hospital Anxiety and Depression Scale; ICD-10, International Classification of Diseases, Tenth Revision; PF, pemphigus foliaceus; PV, pemphigus vulgaris; QOL, quality of life.

of psychological symptoms. Clinicians should be mindful of this at-risk population and create opportunities in clinic to discuss personal hardship associated with the disease process and recommend psychiatric intervention if indicated. Additionally, family members often are overburdened with the chronicity of ABDs, and they should not be forgotten. Using one of the aforementioned questionnaires is a practical way to screen patients for lower QOL scores. We agree with Paradisi and colleagues¹⁹ that although these questionnaires may be helpful, clinicians still need to determine if the use of a

dermatologic QOL evaluation tool in clinical practice improves patient satisfaction.

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